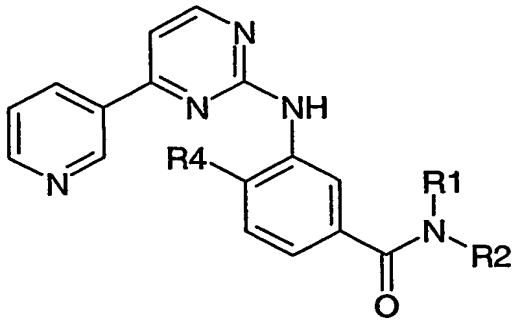
WHAT IS CLAIMED IS:

1. A compound of formula



(I)

wherein

R_1 represents hydrogen, lower alkyl, lower alkoxy-lower alkyl, acyloxy-lower alkyl, carboxy-lower alkyl, lower alkoxycarbonyl-lower alkyl, or phenyl-lower alkyl;

R_2 represents hydrogen, lower alkyl, optionally substituted by one or more identical or different radicals R_3, cycloalkyl, benzcycloalkyl, heterocyclyl, an aryl group, or a mono- or bicyclic heteroaryl group comprising zero, one, two or three ring nitrogen atoms and zero or one oxygen atom and zero or one sulfur atom, which groups in each case are unsubstituted or mono- or polysubstituted; and

R_3 represents hydroxy, lower alkoxy, acyloxy, carboxy, lower alkoxycarbonyl, carbamoyl, N-mono- or N,N-disubstituted carbamoyl, amino, mono- or disubstituted amino, cycloalkyl, heterocyclyl, an aryl group, or a mono- or bicyclic heteroaryl group comprising zero, one, two or three ring nitrogen atoms and zero or one oxygen atom and zero or one sulfur atom, which groups in each case are unsubstituted or mono- or polysubstituted; or wherein

R_1 and R_2 together represent alkylene with four, five or six carbon atoms optionally mono- or disubstituted by lower alkyl, cycloalkyl, heterocyclyl, phenyl, hydroxy, lower alkoxy, amino, mono- or disubstituted amino, oxo, pyridyl, pyrazinyl or pyrimidinyl; benzalkylene with four or five carbon atoms; oxaalkylene with one oxygen and three or four carbon atoms; or azaalkylene with one nitrogen and three or four carbon atoms wherein nitrogen is unsubstituted or substituted by lower alkyl, phenyl-lower alkyl, lower alkoxycarbonyl-lower alkyl, carboxy-lower alkyl, carbamoyl-lower alkyl, N-mono- or N,N-disubstituted carbamoyl-lower alkyl, cycloalkyl, lower alkoxycarbonyl, carboxy, phenyl, substituted phenyl, pyridinyl, pyrimidinyl, or pyrazinyl;

R_4 represents hydrogen, lower alkyl, or halogen;

and a N-oxide or a pharmaceutically acceptable salt of such a compound.

2. A compound of formula I according to claim 1 wherein

R_1 represents hydrogen, lower alkyl, lower alkoxy-lower alkyl, acyloxy-lower alkyl, carboxy-lower alkyl, lower alkoxycarbonyl-lower alkyl, or phenyl-lower alkyl;

R_2 represents hydrogen, lower alkyl, optionally substituted by one or two identical or different radicals R_3, cycloalkyl, benzcycloalkyl, heterocyclyl, an aryl group, or a mono- or bicyclic heteroaryl group comprising one, two or three nitrogen atoms or one sulfur atom, which aryl and heteroaryl groups in each case are unsubstituted or mono- or polysubstituted; and

R_3 represents hydroxy, lower alkoxy, acyloxy, carboxy, lower alkoxycarbonyl, carbamoyl, N-mono- or N,N-disubstituted carbamoyl, amino, mono- or disubstituted amino, cycloalkyl, heterocyclyl, an aryl group, furanoyl, thienoyl, or a mono- or bicyclic heteroaryl group comprising one, two or three ring nitrogen atoms, zero or one ring oxygen atom and zero or one ring sulphur atom, which aryl and heteroaryl groups in each case are unsubstituted or mono- or polysubstituted; or wherein

R_1 and R_2 together represent alkylene with four or five carbon atoms, optionally mono- or disubstituted by lower alkyl, cycloalkyl, heterocyclyl, phenyl, hydroxy, lower alkoxy, amino, mono- or disubstituted amino, pyridyl, pyrazinyl or pyrimidinyl; benzalkylene with four or five carbon atoms in the alkylene group; oxaalkylene with one oxygen and three or four carbon atoms, or azaalkylene with one nitrogen and three or four carbon atoms wherein nitrogen is unsubstituted or substituted by lower alkyl, phenyl-lower alkyl, lower alkoxycarbonyl-lower alkyl, carboxy-lower alkyl, carbamoyl-lower alkyl, N-mono- or N,N-disubstituted carbamoyl-lower alkyl, cycloalkyl, lower alkoxycarbonyl, phenyl, substituted phenyl, pyridinyl, pyrimidinyl, or pyrazinyl;

R_4 represents hydrogen, lower alkyl, or halogen;

and a N-oxide or a pharmaceutically acceptable salt of such a compound.

3. A compound of formula I according to claim 1 wherein

R_1 represents hydrogen, lower alkyl, lower alkoxy-lower alkyl, lower alkoxycarbonyl-lower alkyl, or phenyl-lower alkyl;

R_2 represents hydrogen, lower alkyl, optionally substituted by one or two identical or different radicals R_3, cyclopentyl, benzcyclopentyl, cylcohexyl, pyrrolidinyl, oxazolinyl, piperidinyl, N-substituted piperidinyl, morpholinyl, azepinyl, oxo-azepinyl, oxazepinyl, phenyl, naphthalinyl, tetrahydronaphthalinyl or a mono- or bicyclic heteroaryl group comprising one

or two nitrogen atoms, which phenyl, naphthalinyl and heteroaryl groups in each case are unsubstituted or mono- or polysubstituted, thienyl, or lower alkoxycarbonyl-lower alkylthienyl; and

R_3 represents hydroxy, lower alkoxy, acyloxy, carboxy, lower alkoxycarbonyl, carbamoyl, N-mono- or N,N-disubstituted carbamoyl, amino, lower alkylamino, di-lower alkylamino, phenylamino, N-lower alkyl-N-phenylamino, pyrrolidino, oxopyrrolidino, piperidino, morpholino, imidazolino, oxoimidazolino, cycloalkyl, heterocyclyl, furyl, phenyl, naphthalinyl, tetrahydronaphthalinyl, or a mono- or bicyclic heteroaryl group comprising one or two nitrogen atoms, which phenyl, naphthalinyl and heteroaryl group are unsubstituted or mono- or polysubstituted; or wherein

R_1 and R_2 together represent alkylene with four or five carbon atoms, optionally mono- or disubstituted by lower alkyl, cycloalkyl, heterocyclyl, phenyl, hydroxy, lower alkoxy, amino, mono- or disubstituted amino, pyridyl, pyrazinyl or pyrimidinyl; benzalkylene with four or five carbon atoms in the alkylene group; oxaalkylene with one oxygen and four carbon atoms; or azaalkylene with one nitrogen and four carbon atoms wherein nitrogen is unsubstituted or substituted by lower alkyl, phenyl-lower alkyl, lower alkoxycarbonyl-lower alkyl, carboxy-lower alkyl, carbamoyl-lower alkyl, N-mono- or N,N-disubstituted carbamoyl-lower alkyl, cycloalkyl, lower alkoxycarbonyl, phenyl, substituted phenyl, pyridinyl, pyrimidinyl, or pyrazinyl;

R_4 represents hydrogen, lower alkyl, or halogen;

and a N-oxide or a pharmaceutically acceptable salt of such a compound.

4. A compound of formula I according to claim 1 wherein

R_1 represents hydrogen, lower alkyl, lower alkoxy-lower alkyl, lower alkoxycarbonyl-lower alkyl, or phenyl-lower alkyl;

R_2 represents hydrogen; lower alkyl, optionally substituted by one radical R_3, by two phenyl groups, by two lower alkoycarbonyl groups, by phenyl and lower alkoxycarbonyl, or by hydroxyphenyl and lower alkoxycarbonyl; cyclopentyl; benzcyclopentyl; cylcohexyl; pyrrolidinyl; oxazolinyl; piperidinyl; N-lower alkylpiperidinyl; N-benzylpiperidinyl; N-pyrimidinylpiperidinyl; morpholinyl; azepinyl; oxo-azepinyl; oxazepinyl; phenyl, naphthalinyl, tetrahydronaphthalinyl or a mono- or bicyclic heteroaryl group comprising one or two nitrogen atoms, which phenyl, naphthalinyl and heteroaryl groups in each case are unsubstituted or substituted by one or two substituents selected from the group consisting of lower alkyl, trifluoro-lower alkyl, hydroxy-lower alkyl, lower alkoxy-lower alkyl, amino-

lower alkyl, lower alkylamino-lower alkyl, di-lower alkylamino-lower alkyl, N-cyclohexyl-N-lower alkylamino-lower alkyl, lower alkoxycarbonylpiperidino-lower alkyl, N-lower alkylpiperazino-lower alkyl, lower alkoxycarbonyl-lower alkyl, hydroxy, lower alkoxy, trifluoro-lower alkoxy, 1H-imidazolyl-lower alkoxy, lower alkanoyloxy, benzoyloxy, carboxy, lower alkoxycarbonyl, carbamoyl, lower alkyl carbamoyl, amino, lower alkanoylamino, benzoylamino, amino mono- or disubstituted by lower alkyl, by hydroxy-lower alkyl or by lower alkoxy-lower alkyl, 1H-imidazolyl, mono- or di-lower alkyl-1H-imidazolyl, pyrrolidino, piperidino, piperazino, N-lower alkylpiperazino, morpholino, sulfamoyl, lower alkylsulfonyl, phenylsulfonyl, lower alkylsulfinyl, phenylsulfinyl, lower alkylthio, phenylthio, phenyl, pyridyl, halogenyl, or benzoyl; thienyl; or lower alkoxycarbonyl-lower alkylthienyl; and

R_3 represents hydroxy, lower alkoxy, acyloxy, carboxy, lower alkoxycarbonyl, carbamoyl, carbamoyl mono-or disubstituted by lower alkyl, phenyl or lower alkylene, amino, lower alkylamino, di-lower alkylamino, phenylamino, N-lower alkyl-N-phenylamino, pyrrolidino, oxopyrrolidino, piperidino, morpholino, imidazolino, oxoimidazolino, cycloalkyl, heterocyclyl, furyl; phenyl, naphthalinyl, tetrahydronaphthalinyl, or a mono- or bicyclic heteroaryl group comprising one or two nitrogen atoms, which phenyl, naphthalinyl and heteroaryl group is unsubstituted or substituted by one or two substituents selected from the group consisting of lower alkyl, trifluoro-lower alkyl, lower alkoxycarbonyl-lower alkyl, hydroxy, lower alkoxy, trifluoro-lower alkoxy, lower alkanoyloxy, benzoyloxy, carboxy, lower alkoxycarbonyl, carbamoyl, amino, lower alkanoylamino, benzoylamino, amino mono- or disubstituted by lower alkyl, by hydroxy-lower alkyl or by loweralkoxy-lower alkyl, pyrrolidino, piperidino, morpholino, piperazino, N-lower alkylpiperazino, N-lower alkoxycarbonylpiperazino, phenyl, pyridyl, 1H-imidazolyl, lower alkyl-1H-imidazolyl, sulfamoyl, lower alkylsulfonyl, phenylsulfonyl, lower alkylsulfinyl, phenylsulfinyl, lower alkylthio, phenylthio, halogenyl, or benzoyl; or wherein

R_1 and R_2 together represent alkylene with four or five carbon atoms, optionally mono- or disubstituted by lower alkyl, cycloalkyl, phenyl, hydroxy, lower alkoxy, amino, benzoylamino, piperidino, pyridyl, pyrazinyl or pyrimidinyl; benzalkylene with four or five carbon atoms in the alkylene group; oxaalkylene with one oxygen and four carbon atoms; or azaalkylene with one nitrogen and four carbon atoms wherein nitrogen is unsubstituted or substituted by lower alkyl, phenyl-lower alkyl, lower alkoxycarbonyl-lower alkyl, carboxy-lower alkyl, carbamoyl-lower alkyl, carbamoyl-lower alkyl N-mono- or N,N-disubstituted by lower alkyl, phenyl, lower alkylene or oxa-lower alkylene, cycloalkyl, lower alkoxycarbonyl,

phenyl, methoxyphenyl, trifluoromethylphenyl, trifluoromethoxyphenyl, pyridinyl, pyrimidinyl, or pyrazinyl;

R_4 represents hydrogen or lower alkyl;

and a N-oxide or a pharmaceutically acceptable salt of such a compound.

5. A compound of formula I according to claim 1 wherein

R_1 represents hydrogen, lower alkyl, lower alkoxy-lower alkyl, or benzyl;

R_2 represents lower alkyl, optionally substituted by one radical R_3, by two phenyl groups, by two lower alkoycarbonyl groups, by phenyl and lower alkoxycarbonyl, or by hydroxyphenyl and lower alkoxycarbonyl; cyclopentyl; benzcyclopentyl; cylcohexyl; pyrrolidinyl; piperidinyl; N-lower alkylpiperidinyl; N-benzylpiperidinyl; N-pyrimidinylpiperidinyl; morpholinyl; azepinyl; oxoazepinyl; phenyl; naphthalinyl; tetrahydronaphthalinyl; pyridyl; lower alkyl-pyridyl; quinolinyl; thienyl; lower alkoxycarbonylmethylthienyl; or phenyl substituted by one or two substituents selected from the group consisting of lower alkyl, trifluoro-lower alkyl, hydroxy-lower alkyl, amino-lower alkyl, lower alkylamino-lower alkyl, di-lower alkylamino-lower alkyl, N-cyclohexyl-N-lower alkylamino-lower alkyl, lower alkoxycarbonylpiperidino-lower alkyl, N-lower alkylpiperazino-lower alkyl, lower alkoxycarbonyl-lower alkyl, hydroxy, lower alkoxy, trifluoro-lower alkoxy, 1H-imidazolyl-lower alkoxy, lower alkanoyloxy, benzoyloxy, carboxy, lower alkoxycarbonyl, carbamoyl, lower alkylcarbamoyl, amino, lower alkanoylamino, benzoylamino, amino mono- or disubstituted by lower alkyl, by hydroxy-lower alkyl or by loweralkoxy-lower alkyl, 1H-imidazolyl, lower alkyl-1H-imidazolyl, pyrrolidino, piperidino, piperazino, N-lower alkylpiperazino, morpholino, sulfamoyl, lower alkylsulfonyl, phenyl, pyridyl, halogenyl, or benzoyl; and

R_3 represents hydroxy, lower alkoxy, lower alkanoyloxy, benzoyloxy, carboxy, lower alkoxycarbonyl, carbamoyl, amino, lower alkylamino, di-lower alkylamino, phenylamino, N-lower alkyl-N-phenylamino, pyrrolidino, oxopyrrolidino, piperidino, morpholino, imidazolino, oxoimidazolino, cyclopropyl, cyclopentyl, cyclohexyl, tetrahydrofuranyl, phenyl, naphthalinyl, tetrahydronaphthalinyl, furyl, a mono- or bicyclic heteroaryl group comprising one or two nitrogen atoms, which heteroaryl group is unsubstituted or mono- or disubstituted by lower alkyl, hydroxy and lower alkoxy, or phenyl substituted by one or two substituents selected from the group consisting of lower alkyl, trifluoro-lower alkyl, lower alkoxycarbonyl-lower alkyl, hydroxy, lower alkoxy, trifluoro-lower alkoxy, lower alkanoyloxy, benzoyloxy, carboxy, lower alkoxycarbonyl, carbamoyl, amino, lower alkanoylamino, benzoylamino, amino mono- or disubstituted by lower alkyl, by hydroxy-lower alkyl or by

loweralkoxy-lower alkyl, pyrrolidino, piperidino, morpholino, piperazino, N-lower alkylpiperazino, N-lower alkoxycarbonylpiperazino, phenyl, pyridyl, 1H-imidazolyl, lower alkyl-1H-imidazolyl, sulfamoyl, lower alkylsulfonyl, halogenyl, or benzoyl; or wherein

R_1 and R_2 together represent alkylene with four or five carbon atoms, optionally mono- or disubstituted by phenyl, hydroxy, amino, benzoylamino, or piperidino; benzalkylene with four or five carbon atoms in the alkylene group; oxaalkylene with one oxygen and four carbon atoms; or azaalkylene with one nitrogen and four carbon atoms wherein nitrogen is unsubstituted or substituted by lower alkyl, phenyl-lower alkyl, lower alkoxycarbonyl-lower alkyl, carbamoyl-lower alkyl, pyrrolidinocarbonyl-lower alkyl, morpholinocarbonyl-lower alkyl, cyclopentyl, lower alkoxycarbonyl, phenyl, methoxyphenyl, trifluoromethylphenyl, pyridinyl; pyrimidinyl, or pyrazinyl;

R_4 represents hydrogen or methyl;

and a N-oxide or a pharmaceutically acceptable salt of such a compound.

6. A compound of formula I according to claim 1 wherein

R_1 represents hydrogen;

R_2 represents phenyl substituted by trifluoromethyl and optionally a further substituent selected from the group consisting of hydroxy-lower alkyl, lower alkylamino, hydroxy-lower alkylamino, di-lower alkylamino, 1H-imidazolyl, lower alkyl-1H-imidazolyl, carbamoyl, lower alkylcarbamoyl, pyrrolidino, piperidino, piperazino, lower alkylpiperazino, morpholino, lower alkoxy, trifluoro-lower alkoxy, phenyl, pyridyl, and halogenyl;

R_4 represents methyl;

and a N-oxide or a pharmaceutically acceptable salt of such a compound.

7. A compound of formula I according to claim 1 wherein

R_1 represents hydrogen;

R_2 represents phenyl substituted by 3-trifluoromethyl and optionally a further substituent selected from the group consisting of 1-hydroxy-1-methylethyl, methylamino, ethylamino, 2-hydroxy-1-propylamino, 2-hydroxy-2-propylamino, diethylamino, 1H-imidazolyl, 2- and 4-methyl-1H-imidazolyl, carbamoyl, methylcarbamoyl, pyrrolidino, piperidino, piperazino, 4-methylpiperazino, morpholino, methoxy, trifluoromethoxy, 2,2,2-trifluoroethoxy, phenyl, 2-, 3- and 4-pyridyl, chloro, and fluoro;

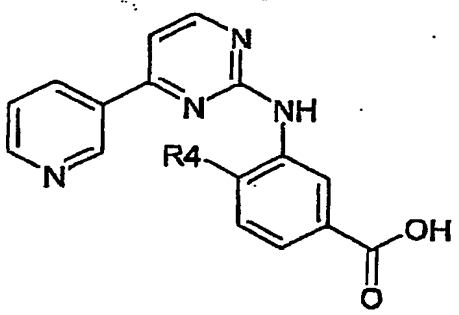
R_4 represents methyl;

and a N-oxide or a pharmaceutically acceptable salt of such a compound.

8. The compound of formula I according to claim 1 wherein
R_1 represents hydrogen;
R_2 represents 3-(1-hydroxy-1-methylethyl)-5-(trifluoromethyl)phenyl;
R_4 represents methyl;
and a N-oxide or a pharmaceutically acceptable salt of such a compound.

9. A compound according to any one of claim 1 wherein
R_1 is hydrogen;
R_2 represents phenyl which is mono- or disubstituted by imidazol-lower alkoxy, lower alkyl amino, trifluoromethyl, hydroxy-lower alkyl amino, bis-(lower alkoxy lower alkyl) amino, lower alkyl piperazinyl, piperidinyl, pyrrolidinyl, morpholinyl, phenyl, pyridyl, imidazolyl which is unsubstituted or mono- or disubstituted by lower alkyl or N-lower alkyl carbamoyl;
R_4 is lower alkyl;
and a N-oxide or a pharmaceutically acceptable salt of such a compound.

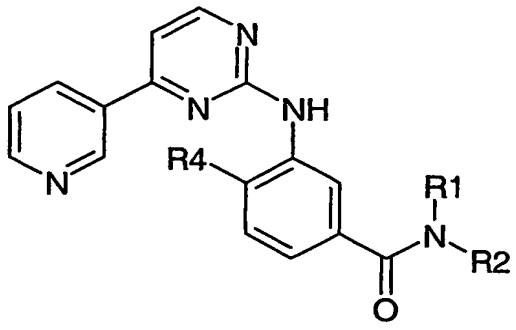
10. A compound of formula



(II)

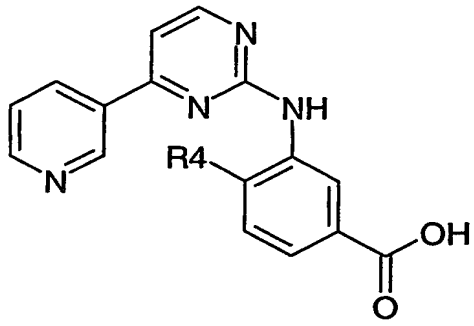
wherein R_4 is methyl.

11. A process for the synthesis of a compound of the formula



(I)

or an N-oxide or a salt thereof, wherein the symbols R_1, R_2 and R_4 are as defined in claim 1, characterized in that a compound of formula II



(II)

wherein R_4 is as defined for a compound of formula I, or a derivative thereof wherein the carboxy group –COOH is in activated form, is reacted with an amine of the formula III

$$R_1\text{-NH-}R_2 \qquad \text{(III)}$$

wherein R_1 and R_2 are as defined for a compound of the formula I, optionally in the presence of a dehydrating agent and an inert base and/or a suitable catalyst, and optionally in the presence of an inert solvent;

where the above starting compounds II and III may also be present with functional groups in protected form if necessary and/or in the form of salts, provided a salt-forming group is present and the reaction in salt form is possible;

any protecting groups in a protected derivative of a compound of the formula I are removed;

and, if so desired, an obtainable compound of formula I is converted into another compound of formula I or a N-oxide thereof, a free compound of formula I is converted into a salt, an obtainable salt of a compound of formula I is converted into the free compound or another

salt, and/or a mixture of isomeric compounds of formula I is separated into the individual isomers.

12. A pharmaceutical composition comprising as an active ingredient a compound of formula I according to any one of claims 1 to 10 or a N-oxide or a pharmaceutically acceptable salt thereof together with a pharmaceutically acceptable carrier.

13. A method for the treatment of a disease which responds to an inhibition of protein kinase activity, which comprises administering a compound of formula I according to any one of claims 1 to 10 or a N-oxide or a pharmaceutically acceptable salt thereof.

14. The use of a compound of formula I according to any one of claims 1 to 10 or a N-oxide or a possible tautomer thereof or of a pharmaceutically acceptable salt thereof for the preparation of a pharmaceutical composition for the treatment of a disease which responds to an inhibition of protein kinase activity.